

## EDITORIAL

## Evaluation of hibernating myocardium

J J Bax, D Poldermans, E E van der Wall

*Heart* 2004;90:1239–1240. doi: 10.1136/hrt.2004.035998

## Identification of hibernating myocardium and subsequent prediction of recovery of function after revascularisation remains intriguing

Over the years, Rahimtoola popularised the term hibernation to describe the situation of chronic obstructive coronary artery disease resulting in chronic contractile dysfunction, which could be reversed after surgical revascularisation.<sup>1</sup> Based on this observation, physicians became aware that chronic left ventricular (LV) dysfunction was not necessarily an irreversible process, and that in the presence of dysfunctional but viable myocardium, recovery of function was possible after revascularisation. In a large observational study, Rahimtoola subsequently demonstrated that this was not a rare phenomenon, but rather this situation occurred frequently in the clinical setting.<sup>2</sup>

Over time, among many other aspects of hibernation, three issues have come to the fore:

- Is resting perfusion reduced or normal in hibernating myocardium?
- Which technique is ideal to detect hibernation and predict recovery of function after revascularisation—in particular, nuclear imaging or dobutamine echocardiography?
- What is the optimal timing to assess recovery of function after revascularisation?

In this issue of *Heart*, Alamanni and colleagues<sup>3</sup> have carefully evaluated 23 patients with chronic LV dysfunction who underwent revascularisation. Usefully, information relating to the above three issues can be derived from this study.

## FLOW RESERVE

At first, hibernating myocardium was considered to have reduced resting blood flow,<sup>2</sup> but recent data demonstrated that patients frequently have normal resting flow. Rather, the flow reserve of these patients was reduced.<sup>4</sup> Over the years, this resulted in an ongoing debate since subsequent studies showed both normal and reduced resting flow in patients with chronic reversible LV dysfunction.<sup>5</sup>

In the study by Alamanni and colleagues,<sup>3</sup> all 23 patients had a chronic left anterior descending coronary artery stenosis without a previous infarction, and all underwent subsequent revascularisation. Using thermodilution techniques, the authors demonstrated a reduced flow in 74% of the patients, whereas in the remaining 26%

resting flow was normal. These findings confirm that resting flow can be normal or reduced.

Initially it was thought that these situations represented two different entities, and the term chronic or repetitive stunning was introduced to describe the situation of chronic LV dysfunction in the presence of normal resting flow,<sup>4</sup> whereas the term hibernation remained reserved for the situation of chronic LV dysfunction in the presence of reduced resting flow. However, recent data from animal experiments demonstrated that initially resting flow may be normal, but that with ongoing ischaemia, resting flow may eventually become reduced.<sup>6</sup> Based on these observations, it was suggested that chronic stunning and hibernation may not be two different entities but rather represent two ends of the spectrum of chronic ischaemia, and that chronic stunning (with normal resting flow) may progress over time to hibernation (with reduced resting flow). In parallel with the reduction in flow, the severity of damage in terms of severity of contractile dysfunction is likely to increase. Indeed, patients with a chronic dysfunction and reduced resting flow have more severe wall motion abnormalities as compared to patients with preserved resting flow.<sup>7</sup> This, however, was not observed in the current study by Alamanni and colleagues<sup>3</sup> since the patients with normal resting flow did not reveal any wall motion abnormalities. Moreover, the entire study population had a rather preserved global LV function.

## PREDICTION OF FUNCTIONAL RECOVERY

Independent of the debate on resting flow, the prediction of improvement in function after revascularisation has become an important issue in the clinical management of patients with chronic LV dysfunction. For this purpose, various non-invasive imaging techniques have been introduced, aimed at the identification of residual viable myocardium in the regions of contractile dysfunction. These techniques include nuclear imaging with positron emission tomography and single photon emission computed tomography, dobutamine echocardiography, and various magnetic resonance imaging techniques.<sup>8</sup> In the clinical setting, most experience has been obtained with nuclear imaging and dobutamine echocardiography.<sup>8</sup> While nuclear imaging relies upon assessment of perfusion, cell membrane integrity, and metabolism, dobutamine echocardiography relies upon assessment of contractile reserve.<sup>8</sup>

Although both modalities can predict improvement of function post-revascularisation, pooled analysis of available studies has demonstrated that nuclear imaging may be more sensitive for the detection of viable myocardium, particularly

See end of article for authors' affiliations

Correspondence to:  
Dr Jeroen J Bax,  
Department of Cardiology,  
Leiden University Medical  
Center, Albnusdreef 2,  
2333 ZA Leiden, The  
Netherlands; j.bax@  
knoware.nl

in patients with severely depressed LV function.<sup>8</sup> For example, Sloof and colleagues<sup>9</sup> demonstrated in a head-to-head comparison in 14 patients that 40–50% of the dysfunctional segments classified as viable on nuclear imaging, were classified as non-viable by stress echocardiography. This phenomenon can be explained as follows. With ongoing ischaemia, and progression from chronic stunning to hibernation, more damage at the myocyte level may occur, including significant damage of the contractile apparatus. In these patients, contractile reserve may no longer be present, although other viability markers, including perfusion, metabolism and cell membrane integrity may still be preserved, explaining the discrepancy between nuclear imaging and dobutamine echocardiography.

In the study by Alamanni and colleagues,<sup>3</sup> both thallium-201 rest-redistribution imaging (aiming at assessment of cell membrane integrity) and dobutamine echocardiography were performed; in agreement with the literature, a higher percentage of dysfunctional segments showed viability on thallium-201 imaging as compared to dobutamine echocardiography (91% v 78%), although the discrepancy was less compared to previous observations. This finding is not completely surprising, since the patients in the present study had a preserved LV function with a relatively short history of disease.

### TIMING OF RECOVERY

Alamanni and colleagues<sup>3</sup> subsequently focused on the timing of improvement of function after revascularisation. For that purpose, LV function was assessed by echocardiography performed immediately after surgery and repeated at one week and three months of follow up. Of interest, the authors demonstrated that the majority of dysfunctional segments improved in contractile function immediately after revascularisation. Currently, not many studies have sequentially (at different time intervals) after revascularisation assessed LV function. The majority of studies focusing on improvement of function post-revascularisation have evaluated LV function approximately three months after revascularisation.<sup>8</sup> In these studies, the prevalence of recovery in function varied substantially, and may be related to differences in study populations.

It is currently unclear, however, at what time the improvement of function occurs. The data by Alamanni and colleagues<sup>3</sup> suggest that improvement of function may occur immediately after surgical restoration of blood flow. However, as indicated before, the patients had only minimal impairment of LV function, whereas 26% of the patients had

no contractile dysfunction at all. In patients with more severely depressed LV function, recovery of contractile function may take longer. In particular, with severe damage at the myocyte level, it has recently been demonstrated that recovery of function may not be completed before one year after revascularisation.<sup>10</sup> It is therefore of interest that a substantial percentage of dysfunctional segments did not exhibit improvement of function at three months after revascularisation, despite the fact that the majority of segments was viable according to the non-invasive imaging techniques. It is possible that recovery of function may have occurred at longer follow up.

In summary, the data provided by Alamanni and colleagues<sup>3</sup> contribute to the ongoing experience in patients with chronic ischaemic LV dysfunction undergoing revascularisation. They also emphasise that a wide spectrum of severity of damage may exist, ranging from minimal damage with preserved blood flow, and early recovery of function, to severe damage with more reduced blood flow and delayed recovery of function after revascularisation.

### Authors' affiliations

J J Bax, E E van der Wall, Department of Cardiology, Leiden University Medical Center, The Netherlands

D Poldermans, ThoraxCenter, Rotterdam, The Netherlands

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